

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

Amendments to the Claims:

This listing of the claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-40 (Cancelled).

41 (Currently Amended). A method for selectively inhibiting abnormal cell proliferation in a subject in need thereof, comprising administering to the subject an amount of an A3-selective adenosine A3 receptor agonist (A3RAg), in a manner such that it exerts its prime effect through the adenosine A3 receptor, the amount being less than 100 µg/Kg body weight ~~effective to selectively inhibit abnormal cell proliferation.~~

42 (Original). A method according to Claim 41, for inhibiting growth or proliferation of tumor cells.

43 (Cancelled)

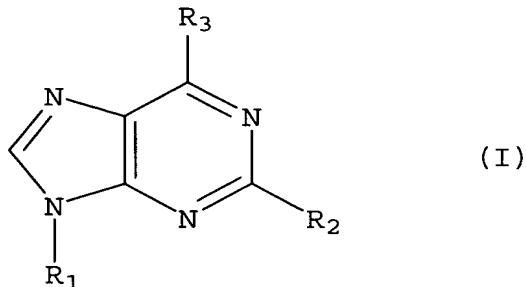
44 (Previously Presented). A method according to Claim 41, wherein the drug is administered orally.

45 (Original). A method according to Claim 41, wherein the drug is administered in combination with a chemotherapeutic drug.

46 (Previously Presented). A method according to Claim 41, wherein said active ingredient is an A3-selective

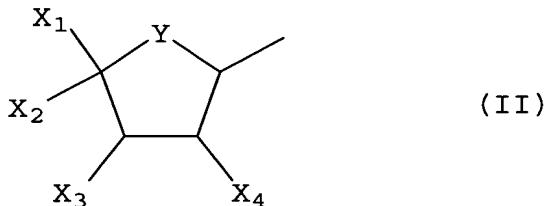
Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

A3RAg that is a nucleoside derivative of the following general formula (I) :



wherein

- R₁ is C₁-C₁₀ alkyl, C₁-C₁₀ hydroxyalkyl, C₁-C₁₀ carboxyalkyl or C₁-C₁₀ cyanoalkyl or a group of the following general formula (II) :



in which:

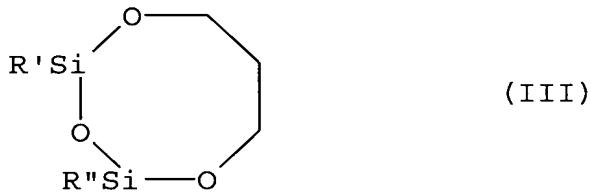
- Y is an oxygen or sulfur atom or CH₂;
- X₁ is H, C₁-C₁₀ alkyl, R^aR^bNC(=O)- or HOR^c-, wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C₁-C₁₀ alkyl, amino, C₁-C₁₀ haloalkyl, C₁-C₁₀ aminoalkyl, C₁-C₁₀ BOC-aminoalkyl, and C₃-C₁₀ cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms, and R^c is selected from

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

the group consisting of C₁-C₁₀ alkyl, amino, C₁-C₁₀ haloalkyl, C₁-C₁₀ aminoalkyl, C₁-C₁₀ BOC-aminoalkyl, and C₃-C₁₀ cycloalkyl;

- X₂ is H, hydroxyl, C₁-C₁₀ alkylamino, C₁-C₁₀ alkylamido or C₁-C₁₀ hydroxyalkyl;

- X₃ and X₄ each independently are hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, -OCOPh, -OC(=S)OPh or both X₃ and X₄ are oxygen connected to >C=S to form a 5-membered ring, or X₂ and X₃ form the ring of formula (III):

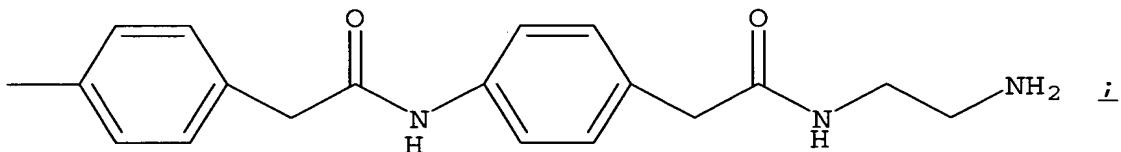


where R' and R'' are independently C₁-C₁₀ alkyl;

- R₂ is selected from the group consisting of hydrogen, halo, C₁-C₁₀ alkylether, amino, hydrazido, C₁-C₁₀ alkylamino, C₁-C₁₀ alkoxy, C₁-C₁₀ thioalkoxy, pyridylthio, C₂-C₁₀ alkenyl; C₂-C₁₀ alkynyl, thio, and C₁-C₁₀ alkylthio; and

- R₃ is a -NR₄R₅ group with R₄ being hydrogen, alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S or NR^a, and, when R₄ is hydrogen, R₅ being selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups, each said group being unsubstituted or substituted in one or more positions with a substituent .

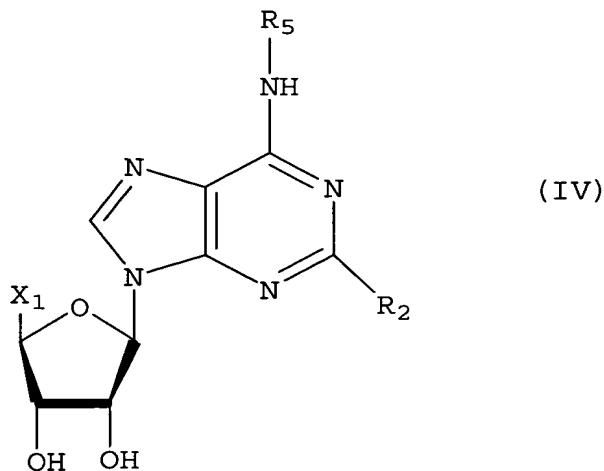
selected from the group consisting of C₁-C₁₀ alkyl, amino, halo, C₁-C₁₀ haloalkyl, nitro, hydroxyl, acetamido, C₁-C₁₀ alkoxy, and sulfonic acid or a salt thereof; or R₅ being benzodioxanemethyl, fururyl, L-propylalanylaminobenzyl, β -alanylaminobenzyl, T-BOC- β -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or C₁-C₁₀ cycloalkyl; or R₅ being a group of the following formula:



or, when R₄ is alkyl, substituted alkyl, or aryl-NH-C(Z)-, then R₅ being selected from the group consisting of substituted or unsubstituted heteroaryl-NR^a-C(Z), heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z);

or a suitable salt of the compound defined above.

47 (Previously Presented). A method according to Claim 46, wherein said active ingredient is an A3-selective A3RAG that is a nucleoside derivative of the general formula (IV) :



in which X_1 , R_2 and R_5 are as defined in Claim 46.

48 (Original). A method according to Claim 47, wherein said active ingredient is an N^6 -benzyladenosine-5'-uronamide.

49 (Previously Presented). A method according to Claim 48, wherein said active ingredient is selected from the group consisting of N^6 -2-(4-aminophenyl)ethyladenosine (APNEA), N^6 -(4-amino-3-iodobenzyl)adenosine-5'-(N -methyluronamide) (AB-MECA) and 1-deoxy-1-{6-[({3-iodophenyl}methyl)amino]-9H-purine-9-yl}- N -methyl- β -D-ribofuranuronamide (IB-MECA) and 2-chloro- N^6 -(3-iodobenzyl)adenosine-5'- N -methyluronamide (Cl-IB-MECA).

50 (Currently Amended). A method for treating cancer in a subject in need thereof, which subject is undergoing chemotherapeutic drug treatment, comprising administering to the subject an amount of an A3-selective

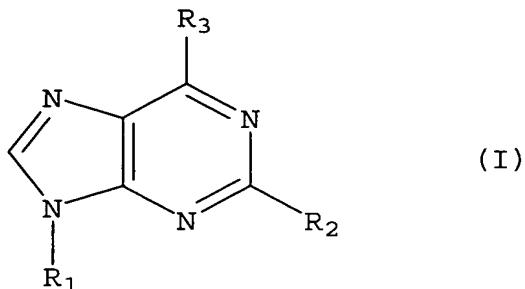
Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

adenosine A3 receptor agonist (A3RAg), in a manner such that it exerts its prime effect through the adenosine A3 receptor, the amount being effective to both selectively inhibit proliferation of cancer cells and to counter toxic side effects of chemotherapeutic drug treatment of the same subject, wherein said amount is less than 100 μ g/Kg body weight.

51 (Currently Amended). A method according to Claim 50, wherein the A3RAg synergizes with said chemotherapeutic drug to yield a stronger anti-tumor effect.

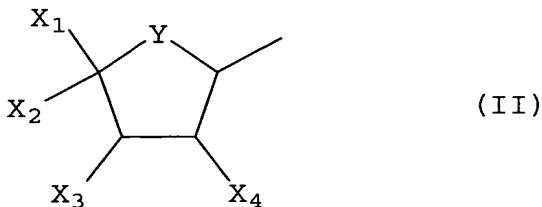
52 (Original). A method according to Claim 50, wherein the drug is administered orally.

53 (Previously Presented). A method according to Claim 50, wherein said active ingredient is an A3-selective A3RAg that is a nucleoside derivative of the following general formula (I):



wherein

- R_1 is C_1-C_{10} alkyl, C_1-C_{10} hydroxyalkyl, C_1-C_{10} carboxyalkyl or C_1-C_{10} cyanoalkyl or a group of the following general formula (II):



in which:

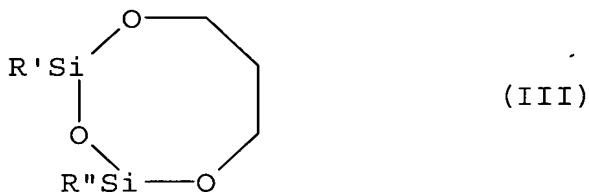
- Y is an oxygen or sulfur atom or CH_2 ;

- X_1 is H, C_1-C_{10} alkyl, $R^aR^bNC(=O)-$ or HOR^c- , wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, C_1-C_{10} BOC-aminoalkyl, and C_3-C_{10} cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms, and R^c is selected from the group consisting of C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, C_1-C_{10} BOC-aminoalkyl, and C_3-C_{10} cycloalkyl;

- X_2 is H, hydroxyl, C_1-C_{10} alkylamino, C_1-C_{10} alkylamido or C_1-C_{10} hydroxyalkyl;

- X_3 and X_4 each independently are hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, $-OCOPh$, $-OC(=S)OPh$ or both X_3 and X_4 are oxygen

connected to >C=S to form a 5-membered ring, or X₂ and X₃ form the ring of formula (III):



where R' and R'' are independently C₁-C₁₀ alkyl;

- R₂ is selected from the group consisting of hydrogen, halo, C₁-C₁₀ alkylether, amino, hydrazido, C₁-C₁₀ alkylamino, C₁-C₁₀ alkoxy, C₁-C₁₀ thioalkoxy, pyridylthio, C₂-C₁₀ alkenyl; C₂-C₁₀ alkynyl, thio, and C₁-C₁₀ alkylthio; and

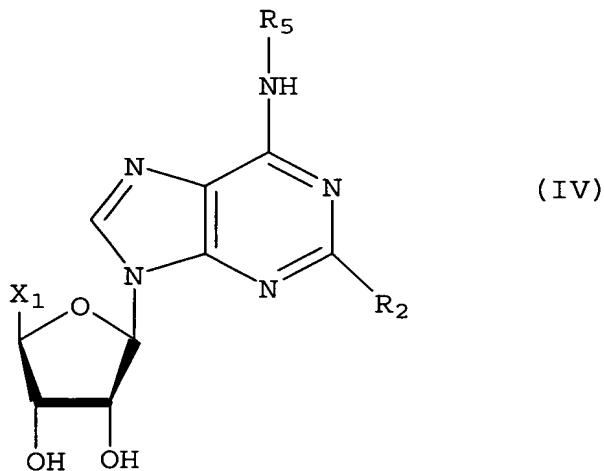
- R₃ is a -NR₄R₅ group with R₄ being hydrogen, alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S or NR^a, and, when R₄ is hydrogen, R₅ being selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups, each said group being unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of C₁-C₁₀ alkyl, amino, halo, C₁-C₁₀ haloalkyl, nitro, hydroxyl, acetamido, C₁-C₁₀ alkoxy, and sulfonic acid or a salt thereof; or R₅ being benzodioxanemethyl, fururyl, L-propylalanylaminobenzyl, β -alanylaminobenzyl, T-BOC- β -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or C₁-C₁₀ cycloalkyl; or R₅ being a group of the following formula:



or, when R_4 is alkyl, substituted alkyl, or aryl-NH-C(Z)-, then R_5 being selected from the group consisting of substituted or unsubstituted heteroaryl-NR^a-C(Z), heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z);

or a suitable salt of the compound defined above.

54 (Previously Presented). A method according to Claim 53, wherein said active ingredient is an A3-selective A3RAG that is a nucleoside derivative of the general formula (IV) :



in which X_1 , R_2 and R_5 are as defined in Claim 53.

55 (Original). A method according to Claim 54, wherein said active ingredient is an N⁶-benzyladenosine-5'-uronamide.

56 (Previously Presented). A method according to Claim 55, wherein said active ingredient is selected from the group consisting of N⁶-2-(4-aminophenyl)ethyladenosine (APNEA), N⁶-(4-amino-3-iodobenzyl)adenosine-5'-(N-methyluronamide) (AB-MECA) and 1-deoxy-1-{6-[({3-iodophenyl}methyl)amino]-9H-purine-9-yl}-N-methyl-β-D-ribofuranuronamide (IB-MECA) and 2-chloro-N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide (Cl-IB-MECA).

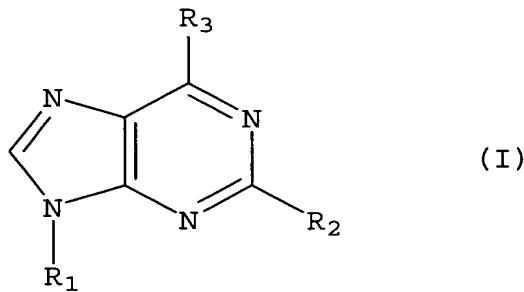
57 (Currently Amended). A method for selectively inhibiting abnormal cell proliferation in a subject, comprising administering to the subject an amount of an adenosine A3 receptor agonist (A3R^{Ag}) in a manner such that it exerts its prime effect through the A3 adenosine receptor without essentially activating adenosine receptors other than the A3 adenosine receptor, the amount being effective to selectively inhibit abnormal cell proliferation.

58 (Previously Presented). A method according to Claim 41, wherein said abnormal cell proliferation is the growth or proliferation of tumor cells.

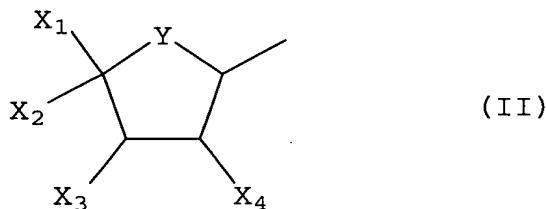
59 (Previously Presented). A method according to Claim 57, wherein the drug is administered orally.

60 (Previously Presented). A method according to
Claim 57, wherein the drug is administered in combination with
a chemotherapeutic drug.

61 (Previously Presented). A method according to
Claim 57, wherein the active ingredient is an A3RAg that
exerts its prime effect through the A3 adenosine receptor
without essentially activating adenosine receptors other than
the A3 adenosine receptor, which is a nucleoside derivative of
the following general formula (I):



wherein R₁ is C₁-C₁₀ alkyl, C₁-C₁₀ hydroxyalkyl, C₁-C₁₀ carboxyalkyl or C₁-C₁₀ cyanoalkyl or a group of the following
general formula (II):



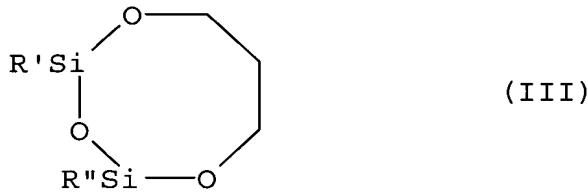
in which:

- Y is an oxygen or sulfur atom or CH₂;

- X_1 is H, C_1-C_{10} alkyl, $R^aR^bNC(=O)-$ or HOR^c- , wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, C_1-C_{10} BOC-aminoalkyl, and C_3-C_{10} cycloalkyl or are joined together to form a heterocyclic ring containing two to five carbon atoms, and R^c is selected from the group consisting of C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, C_1-C_{10} BOC-aminoalkyl, and C_3-C_{10} cycloalkyl;

- X_2 is H, hydroxyl, C_1-C_{10} alkylamino, C_1-C_{10} alkylamido or C_1-C_{10} hydroxyalkyl;

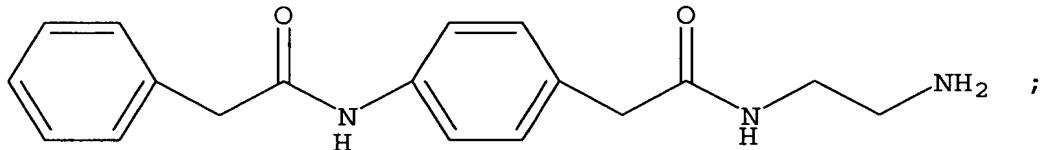
- X_3 and X_4 each independently are hydrogen, hydroxyl, amino, amido, azido, halo, alkyl, alkoxy, carboxy, nitrilo, nitro, trifluoro, aryl, alkaryl, thio, thioester, thioether, $-OCOPh$, $-OC(=S)OPh$ or both X_3 and X_4 are oxygen connected to $>C=S$ to form a 5-membered ring, or X_2 and X_3 form the ring of formula (III):



where R' and R'' are independently C_1-C_{10} alkyl;

- R_2 is selected from the group consisting of hydrogen, halo, C_1-C_{10} alkylether, amino, hydrazido, C_1-C_{10} alkylamino, C_1-C_{10} alkoxy, C_1-C_{10} thioalkoxy, pyridylthio, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, thio, and C_1-C_{10} alkylthio; and

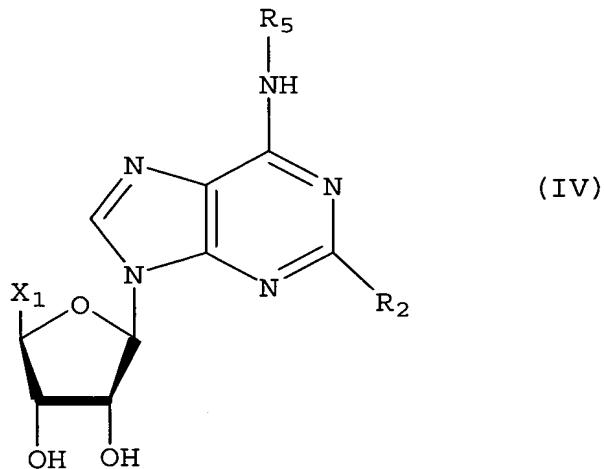
- R_3 is a $-NR_4R_5$ group with R_4 being hydrogen, alkyl, substituted alkyl or aryl-NH-C(Z)-, with Z being O, S or NR^a , and, when R_4 is hydrogen, R_5 being selected from the group consisting of R- and S-1-phenylethyl, benzyl, phenylethyl or anilide groups, each said group being unsubstituted or substituted in one or more positions with a substituent selected from the group consisting of C_1-C_{10} alkyl, amino, halo, C_1-C_{10} haloalkyl, nitro, hydroxyl, acetamido, C_1-C_{10} alkoxy, and sulfonic acid or a salt thereof; or R_5 being benzodioxanemethyl, fururyl, L-propylalanyl-aminobenzyl, β -alanyl amino-benzyl, T-BOC- β -alanylaminobenzyl, phenylamino, carbamoyl, phenoxy or C_1-C_{10} cycloalkyl; or R_5 being a group of the following formula:



or, when R_4 is alkyl, substituted alkyl, or aryl-NH-C(Z)-, then R_5 is selected from the group consisting of substituted or unsubstituted heteroaryl-NR^a-C(Z)-, heteroaryl-C(Z)-, alkaryl-NR^a-C(Z)-, alkaryl-C(Z)-, aryl-NR-C(Z)- and aryl-C(Z)-; or a suitable salt of said nucleotide derivative.

62 (Previously Presented). A method according to Claim 61, wherein said active ingredient is an A3RAg that exerts its prime effect through the A3 adenosine receptor

without essentially activating adenosine receptors other than the A3 adenosine receptor, which is a nucleoside derivative of the general formula (IV) :



in which X₁, R₂ and R₄ are as defined in Claim 61.

63 (Previously Presented). A method according to Claim 62, wherein said active ingredient is an N6-benzyladenosine-5'-uronamide.

64 (Previously Presented). A method according to Claim 63, wherein said active ingredient is selected from the group consisting of N⁶-2-(4-aminophenyl)ethyladenosine (APNEA), N⁶-(4-amino-3-iodobenzyl) adenosine-5'- (N-methyluronamide) (AB-MECA) and 1-deoxy-1-{6-[(3-iodophenyl) methyl]amino}-9H-purine-9-yl}-N-methyl-β-D-ribofuranuron-amide (IB-MECA) and 2-chloro-N⁶-(3-iodobenzyl)-adenosine-5'-N-methly-uronamide (Cl-IB-MECA).

65 (Previously Presented). A method according to
Claim 57, wherein the active ingredient is administered at an
amount less than 100 μ g/Kg body weight.

66 (Previously Presented). A method according to
Claim 65, wherein the amount is less than 50 μ g/Kg body
weight.

67 (Previously Presented). A method according to
claim 15, wherein said active ingredient is selected from the
group consisting of:

N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-hydroxyethyladenine;
 $R-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 $S-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 N^6 -(3-iodobenzyladenin-9-yl)acetic acid;
 N^6 -(3-iodobenzyl)-9-(3-cyanopropyl)adenine;
2-chloro- N^6 -(3-iodobenzyl)-9-methyladenine;
2-amino- N^6 -(3-iodobenzyl)-9-methyladenine;
2-hydrazido- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methylamino-9-methyladenine;
2-dimethylamino- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-propylaminoadenine;
2-hexylamino- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methoxy-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-methylthioadenine;

N^6 -(3-iodobenzyl)-9-methyl-2-(4-pyridylthio)adenine;
(1S,2R,3S,4R)-4-(6-amino-2-phenylethylamino-9H-purin-9-yl)cyclopentane-1,2,3-triol;
(1S,2R,3S,4R)-4-(6-amino-2-chloro-9H-purin-9-yl)cyclopentane-1,2,3-triol;
(\pm)-9-[2 α ,3 α -dihydroxy-4 β -(N-methylcarbamoyl)cyclopent-1 β -yl]- N^6 -(3-iodobenzyl)-adenine;
2-chloro-9-(2'-amino-2',3'-dideoxy- β -D-5'-methylarabino-furonamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(2',3'-dideoxy-2'-fluoro- β -D-5'-methylarabino-furonamido)- N^6 -(3-iodobenzyl)adenine;
9-(2-acetyl-3-deoxy- β -D-5-methyl-ribofuronamido)-2-chloro- N^6 (3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy-2-methanesulfonyl- β -D-5-methylribofuronamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy- β -D-5-methyl-ribofuronamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(3,5-1,1,3,3-tetraisopropyldisiloxyl- β -D-5-ribofuranosyl)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(2',3'-O-thiocarbonyl- β -D-5-methylribofuronamido)- N^6 -(3-iodobenzyl)adenine;

9- (2-phenoxythiocarbonyl-3-deoxy- β -D-5-methyl-
ribofuronamido)-2-chloro-N⁶- (3-
iodobenzyl)adenine;

1- (6-benzylamino-9H-purin-9-yl)-1-deoxy-N,4-
dimethyl- β -D-ribofuranosiduronamide;

2-chloro-9- (2,3-dideoxy- β -D-5-methyl-
ribofuronamido)-N⁶-benzyladenine;

2-chloro-9- (2'-azido-2',3'-dideoxy- β -D-5'-methyl-
arabino-furonamido)-N⁶-benzyladenine;

2-chloro-9- (β -D-erythrocycluronamide)-N⁶- (3-
iodobenzyl)adenine;

N⁶- (benzodioxanemethyl)adenosine;

1- (6-furfurylamino-9H-purin-9-yl)-1-deoxy-N-methyl-
 β -D-ribofuranosiduronamide;

N⁶- [3- (L-prolylamino)benzyl]adenosine-5'-N-
methyluronamide;

N⁶- [3- (β -alanylamino)benzyl]adenosine-5'-N-
methyluronamide;

N⁶- [3- (N-T-Boc- β -alanylamino)benzyl]adenosine-5'-N-
methyluronamide

6- (N'-phenylhydrazinyl)purine-9- β -ribofuranoside-5'-
N-methyluronamide;

6- (O-phenylhydroxylamino)purine-9- β -ribofuranoside-
5'-N-methyluronamide;

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

9- (β -D-2',3'-dideoxyerythrofuranosyl) -N⁶- [(3- β -alanyl amino) benzyl] adenosine;
9- (β -D-erythrofuranoside) -2-methylamino-N⁶- (3-iodobenzyl) adenine;
2-chloro-N- (3-iodobenzyl) -9- (2-tetrahydrofuryl) -9H-purin-6-amine;
2-chloro- (2'-deoxy-6'-thio-L-arabinosyl) adenine;
2-chloro- (6'-thio-L-arabinosyl) adenine;
N⁶- (4-biphenyl-carbonylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (2,4-dichlorobenzyl-carbonylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (4-methoxyphenyl-carbonylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (4-chlorophenyl-carbonylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (phenyl-carbonylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (benzylcarbamoylamino) -adenosine-5'-N-ethyluronamide;
N⁶- (4-sulfonamido-phenylcarbamoyl) -adenosine-5'-N-ethyluronamide;
N⁶- (4-acetyl-phenylcarbamoyl) -adenosine-5'-N-ethyluronamide;

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

N^6 -((R)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -((S)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -(5-methyl-isoxazol-3-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -(1,3,4-thiadiazol-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -(4-n-propoxy-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -bis-(4-nitrophenylcarbamoyl)-adenosine-5'-N-ethyluronamide; and
 N^6 -bis-(5-chloro-pyridin-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide.

68 (Previously Presented). A method according to Claim 16, wherein said active ingredient is an A3 selective A3R_{Ag} that is selected from the group consisting of those of formula (IV) in which:

X_1 is $R^aR^bNC(=O)$, wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, and C_3-C_{10} cycloalkyl, R_2 is selected from the group consisting of hydrogen, halo, C_1-C_{10} alkoxy, amino, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, and R_5 is selected from the group

consisting of R- and S-1-phenylethyl, an unsubstituted benzyl group, and a benzyl group substituted in one or more positions with a substituent selected from the group consisting of C₁-C₁₀ alkyl, amino, halo, C₁-C₁₀ haloalkyl, nitro, hydroxy, acetamido, C₁-C₁₀ alkoxy, and sulfo.

69 (Previously Presented). A method according to claim 68, wherein said active ingredient is an A3 selective A3RAg that is selected from the group consisting of those of formula (IV) in which:

R^a and R^b are the same or different and are selected from the group consisting of hydrogen and C₁-C₁₀ alkyl, and R₂ is hydrogen or halo;

R^a is hydrogen, R₂ is hydrogen and R₅ is unsubstituted benzyl;

R^b is C₁-C₁₀ alkyl or C₃-C₁₀ cycloalkyl and R₅ in R- or S-1-phenylethyl or a benzyl substituted in one or more positions with a substituent selected from the group consisting of halo, amino, acetamido, C₁-C₁₀ haloalkyl and sulfo, wherein the sulfo derivative is a salt;

R₂ is a C₂-C₁₀ alkyne of the formula R^d-C=C- where R^d is a C₁-C₈ alkyl; or

R₂ is a halo, C₁-C₁₀ alkylamino, or C₁-C₁₀ alkylthio, R^a is hydrogen, R^b is C₁-C₁₀ alkyl and R₅ is a substituted benzyl.

70 (Previously Presented). A method according to
Claim 15, wherein the active ingredient is an A3 selective
A3RAg that is in the form of a triethylammonium salt.

71 (Previously Presented). A method according to
claim 46, wherein said active ingredient is selected from the
group consisting of:

N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-hydroxyethyladenine;
 $R-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 $S-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 N^6 -(3-iodobenzyladenin-9-yl)acetic acid;
 N^6 -(3-iodobenzyl)-9-(3-cyanopropyl)adenine;
2-chloro- N^6 -(3-iodobenzyl)-9-methyladenine;
2-amino- N^6 -(3-iodobenzyl)-9-methyladenine;
2-hydrazido- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methylamino-9-methyladenine;
2-dimethylamino- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-propylaminoadenine;
2-hexylamino- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methoxy-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-methylthioadenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-(4-pyridylthio)adenine;
(1S,2R,3S,4R)-4-(6-amino-2-phenylethylamino-9H-purin-9-yl)cyclopentane-1,2,3-triol;

(1*S*,2*R*,3*S*,4*R*)-4-(6-amino-2-chloro-9*H*-purin-9-yl)-cyclopentane-1,2,3-triol;
(\pm)-9-[2 α ,3 α -dihydroxy-4 β -(N-methylcarbamoyl)cyclopent-1 β -yl)]-N⁶-(3-iodobenzyl)-adenine;
2-chloro-9-(2'-amino-2',3'-dideoxy- β -D-5'-methyl-arabino-furonamido)-N⁶-(3-iodobenzyl)adenine;
2-chloro-9-(2',3'-dideoxy-2'-fluoro- β -D-5'-methyl-arabino-furonamido)-N⁶-(3-iodobenzyl)adenine;
9-(2-acetyl-3-deoxy- β -D-5-methyl-ribofuronamido)-2-chloro-N⁶(3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy-2-methanesulfonyl- β -D-5-methyl-ribofuronamido)-N⁶-(3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy- β -D-5-methyl-ribofuronamido)-N⁶-(3-iodobenzyl)adenine;
2-chloro-9-(3,5-1,1,3,3-tetraisopropyldisiloxyl- β -D-5-ribofuranosyl)-N⁶-(3-iodobenzyl)adenine;
2-chloro-9-(2',3'-O-thiocarbonyl- β -D-5-methyl-ribofuronamido)-N⁶-(3-iodobenzyl)adenine;
9-(2-phenoxythiocarbonyl-3-deoxy- β -D-5-methyl-ribofuronamido)-2-chloro-N⁶-(3-iodobenzyl)adenine;
1-(6-benzylamino-9*H*-purin-9-yl)-1-deoxy-N,4-dimethyl- β -D-ribofuranosiduronamide;

2-chloro-9-(2,3-dideoxy- β -D-5-methyl-ribofuranamido)-N⁶-benzyladenine;

2-chloro-9-(2'-azido-2',3'-dideoxy- β -D-5'-methyl-arabino-furonamido)-N⁶-benzyladenine;

2-chloro-9-(β -D-erythrocyclonoside)-N⁶-(3-iodobenzyl)adenine;

N⁶-(benzodioxanemethyl)adenosine;

1-(6-furfurylaminio-9H-purin-9-yl)-1-deoxy-N-methyl- β -D-ribofuranosiduronamide;

N⁶-[3-(L-prolylaminio)benzyl]adenosine-5'-N-methyluronamide;

N⁶-[3-(β -alanylaminio)benzyl]adenosine-5'-N-methyluronamide;

N⁶-[3-(N-T-Boc- β -alanylaminio)benzyl]adenosine-5'-N-methyluronamide

6-(N'-phenylhydrazinyl)purine-9- β -ribofuranoside-5'-N-methyluronamide;

6-(O-phenylhydroxylaminio)purine-9- β -ribofuranoside-5'-N-methyluronamide;

9-(β -D-2',3'-dideoxyerythrocyclonosyl)-N⁶-[(3- β -alanylaminio)benzyl]adenosine;

9-(β -D-erythrocyclonoside)-2-methylamino-N⁶-(3-iodobenzyl)adenine;

2-chloro-N-(3-iodobenzyl)-9-(2-tetrahydrofuryl)-9H-purin-6-amine;

2-chloro-(2'-deoxy-6'-thio-L-arabinosyl)adenine;

2-chloro-(6'-thio-L-arabinosyl)adenine;

N⁶-(4-biphenyl-carbonylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(2,4-dichlorobenzyl-carbonylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(4-methoxyphenyl-carbonylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(4-chlorophenyl-carbonylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(phenyl-carbonylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(benzylcarbamoylamino)-adenosine-5'-N-ethyluronamide;

N⁶-(4-sulfonamido-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶-(4-acetyl-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶-((R)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶-((S)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

N^6 -(5-methyl-isoxazol-3-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -(1,3,4-thiadiazol-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -(4-n-propoxy-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;
 N^6 -bis-(4-nitrophenylcarbamoyl)-adenosine-5'-N-ethyluronamide; and
 N^6 -bis-(5-chloro-pyridin-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide.

72 (Previously Presented). A method according to claim 53, wherein said active ingredient is selected from the group consisting of:

N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-hydroxyethyladenine;
 $R-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 $S-N^6$ -(3-iodobenzyl)-9-(2,3-dihydroxypropyl)adenine;
 N^6 -(3-iodobenzyladenin-9-yl)acetic acid;
 N^6 -(3-iodobenzyl)-9-(3-cyanopropyl)adenine;
2-chloro- N^6 -(3-iodobenzyl)-9-methyladenine;
2-amino- N^6 -(3-iodobenzyl)-9-methyladenine;
2-hydrazido- N^6 -(3-iodobenzyl)-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methylamino-9-methyladenine;
2-dimethylamino- N^6 -(3-iodobenzyl)-9-methyladenine;

N^6 -(3-iodobenzyl)-9-methyl-2-propylaminoadenine;
 N^6 -(3-iodobenzyl)-2-hexylamino-9-methyladenine;
 N^6 -(3-iodobenzyl)-2-methoxy-9-methyladenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-methylthioadenine;
 N^6 -(3-iodobenzyl)-9-methyl-2-(4-pyridylthio)adenine;
(1S,2R,3S,4R)-4-(6-amino-2-phenylethylamino-9H-purin-9-yl)cyclopentane-1,2,3-triol;
(1S,2R,3S,4R)-4-(6-amino-2-chloro-9H-purin-9-yl)cyclopentane-1,2,3-triol;
(\pm)-9-[2 α ,3 α -dihydroxy-4 β -(N-methylcarbamoyl)cyclopent-1 β -yl]- N^6 -(3-iodobenzyl)-adenine;
2-chloro-9-(2'-amino-2',3'-dideoxy- β -D-5'-methylarabino-furonamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(2',3'-dideoxy-2'-fluoro- β -D-5'-methylarabino-furonamido)- N^6 -(3-iodobenzyl)adenine;
9-(2-acetyl-3-deoxy- β -D-5-methyl-ribofuronamido)-2-chloro- N^6 (3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy-2-methanesulfonyl- β -D-5-methylribofuronamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(3-deoxy- β -D-5-methyl-ribofuronamido)- N^6 -(3-iodobenzyl)adenine;
2-chloro-9-(3,5-1,1,3,3-tetraisopropylsilyl- β -D-5-ribofuranosyl)- N^6 -(3-iodobenzyl)adenine;

Appln. No. 09/700,751
Amdt. dated June 27, 2005
Reply to Office action of June 8, 2005

2-chloro-9-(2',3'-O-thiocarbonyl- β -D-5-methyl-ribofuranamido)-N⁶-(3-iodobenzyl)adenine;
9-(2-phenoxythiocarbonyl-3-deoxy- β -D-5-methyl-ribofuranamido)-2-chloro-N⁶-(3-iodobenzyl)adenine;
1-(6-benzylamino-9H-purin-9-yl)-1-deoxy-N,4-dimethyl- β -D-ribofuranosiduronamide;
2-chloro-9-(2,3-dideoxy- β -D-5-methyl-ribofuranamido)-N⁶-benzyladenine;
2-chloro-9-(2'-azido-2',3'-dideoxy- β -D-5'-methyl-arabino-furonamido)-N⁶-benzyladenine;
2-chloro-9-(β -D-erythrocyclururonamide)-N⁶-(3-iodobenzyl)adenine;
N⁶-(benzodioxanemethyl)adenosine;
1-(6-furfurylamino-9H-purin-9-yl)-1-deoxy-N-methyl- β -D-ribofuranosiduronamide;
N⁶-[3-(L-prolylamino)benzyl]adenosine-5'-N-methylururonamide;
N⁶-[3-(β -alanylaminobenzyl]adenosine-5'-N-methylururonamide;
N⁶-[3-(N-T-Boc- β -alanylaminobenzyl]adenosine-5'-N-methylururonamide
6-(N'-phenylhydrazinyl)purine-9- β -ribofuranoside-5'-N-methylururonamide;

6- (O-phenylhydroxylamino)purine-9- β -ribofuranoside-
5'-N-methyluronamide;
9- (β -D-2',3'-dideoxyerythrocyclurone) -N⁶- [(3- β -
alanylaminobenzyl]adenosine;
9- (β -D-erythrocyclurone) -2-methylaminino-N⁶- (3-
iodobenzyl)adenine;
2-chloro-N- (3-iodobenzyl) -9- (2-tetrahydrofuryl) -9H-
purin-6-amine;
2-chloro- (2'-deoxy-6'-thio-L-arabinosyl)adenine;
2-chloro- (6'-thio-L-arabinosyl)adenine;
N⁶- (4-biphenyl-carbonylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (2,4-dichlorobenzyl-carbonylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (4-methoxyphenyl-carbonylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (4-chlorophenyl-carbonylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (phenyl-carbonylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (benzylcarbamoylamino) -adenosine-5'-N-
ethyluronamide;
N⁶- (4-sulfonamido-phenylcarbamoyl) -adenosine-5'-N-
ethyluronamide;

N⁶- (4-acetyl-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶- ((R)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶- ((S)- α -phenylethylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶- (5-methyl-isoxazol-3-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶- (1,3,4-thiadiazol-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶- (4-n-propoxy-phenylcarbamoyl)-adenosine-5'-N-ethyluronamide;

N⁶-bis-(4-nitrophenylcarbamoyl)-adenosine-5'-N-ethyluronamide; and

N⁶-bis-(5-chloro-pyridin-2-yl-carbamoyl)-adenosine-5'-N-ethyluronamide.

73 (Previously Presented). A method according to Claim 46, wherein the active ingredient is an A3 selective A3RAg that is in the form of a triethylammonium salt.

74 (Previously Presented). A method according to Claim 53, wherein the active ingredient is an A3 selective A3RAg that is in the form of a triethylammonium salt.

75 (Previously Presented). A method according to Claim 47, wherein said active ingredient is an A3 selective

A3R₄ that is selected from the group consisting of those of formula (IV) in which:

X₁ is R^aR^bNC(=O), wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C₁-C₁₀ alkyl, amino, C₁-C₁₀ haloalkyl, C₁-C₁₀ aminoalkyl, and C₃-C₁₀ cycloalkyl, R₂ is selected from the group consisting of hydrogen, halo, C₁-C₁₀ alkoxy, amino, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl, and R₄ is selected from the group consisting of R- and S-1-phenylethyl, an unsubstituted benzyl group, and a benzyl group substituted in one or more positions with a substituent selected from the group consisting of C₁-C₁₀ alkyl, amino, halo, C₁-C₁₀ haloalkyl, nitro, hydroxy, acetamido, C₁-C₁₀ alkoxy, and sulfo.

76 (Previously Presented). A method according to claim 75, wherein said active ingredient is an A3 selective A3R₄ that is selected from the group consisting of those of formula (IV) in which:

R^a and R^b are the same or different and are selected from the group consisting of hydrogen and C₁-C₁₀ alkyl, and R₂ is hydrogen or halo;

R^a is hydrogen, R₂ is hydrogen and R₅ is unsubstituted benzyl;

R^b is C₁-C₁₀ alkyl or C₃-C₁₀ cycloalkyl and R₅ in R- or S-1-phenylethyl or a benzyl substituted in one or more

positions with a substituent selected from the group consisting of halo, amino, acetamido, C_1-C_{10} haloalkyl and sulfo, wherein the sulfo derivative is a salt;

R_2 is a C_2-C_{10} alkyne of the formula $R^d-C=C-$ where R^d is a C_1-C_8 alkyl; or

R_2 is a halo, C_1-C_{10} alkylamino, or C_1-C_{10} alkylthio, R^a is hydrogen, R^b is C_1-C_{10} alkyl and R_5 is a substituted benzyl.

77 (Previously Presented). A method according to Claim 54, wherein said active ingredient is an A3 selective A3RAG that is selected from the group consisting of those of formula (IV) in which:

X_1 is $R^aR^bNC(=O)$, wherein R^a and R^b may be the same or different and are selected from the group consisting of hydrogen, C_1-C_{10} alkyl, amino, C_1-C_{10} haloalkyl, C_1-C_{10} aminoalkyl, and C_3-C_{10} cycloalkyl, R_2 is selected from the group consisting of hydrogen, halo, C_1-C_{10} alkoxy, amino, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, and R_4 is selected from the group consisting of R- and S-1-phenylethyl, an unsubstituted benzyl group, and a benzyl group substituted in one or more positions with a substituent selected from the group consisting of C_1-C_{10} alkyl, amino, halo, C_1-C_{10} haloalkyl, nitro, hydroxy, acetamido, C_1-C_{10} alkoxy, and sulfo.

78 (Previously Presented). A method according to claim 77, wherein said active ingredient is an A3 selective A3R_{Ag} that is selected from the group consisting of those of formula (IV) in which:

R^a and R^b are the same or different and are selected from the group consisting of hydrogen and C₁-C₁₀ alkyl, and R₂ is hydrogen or halo;

R^a is hydrogen, R₂ is hydrogen and R₅ is unsubstituted benzyl;

R^b is C₁-C₁₀ alkyl or C₃-C₁₀ cycloalkyl and R₅ in R- or S-1-phenylethyl or a benzyl substituted in one or more positions with a substituent selected from the group consisting of halo, amino, acetamido, C₁-C₁₀ haloalkyl and sulfo, wherein the sulfo derivative is a salt;

R₂ is a C₂-C₁₀ alkyne of the formula R^d-C=C- where R^d is a C₁-C₈ alkyl; or

R₂ is a halo, C₁-C₁₀ alkylamino, or C₁-C₁₀ alkylthio, R^a is hydrogen, R^b is C₁-C₁₀ alkyl and R₅ is a substituted benzyl.

79 (Previously Presented). A method for inhibiting abnormal cell proliferation in a subject in need thereof, comprising administering to the subject an adenosine A3 receptor agonist (A3R_{Ag}) in an amount of less than 100 μg/Kg body weight.

80 (Previously Presented). A method according to
Claim 79 wherein the amount of the A3RAg is less than 50 μ g/kg
body weight.

81 (New). A method according to claim 41, wherein
said abnormal cell proliferation is associated with an
autoimmune disease.

82 (New). A method according to claim 57, wherein
said abnormal cell proliferation is associated with an
autoimmune disease.